**Amendments to the Claims:**

The following listing of Claims will replace all prior versions and listings of Claims in the Application.

**Listing of the Claims:**

**1**. (Withdrawn) A genetically-modified, non-human mammal comprising an α2/δ1 gene comprising an R217-like mutation.

**2**. (Withdrawn) A genetically-modified, non-human mammal, wherein the modification results in a mutated α2/δ1 gene encoding a polypeptide selected from the group consisting of:

a) An α2/δ1 polypeptide comprising an arginine to non-arginine substitution in at least one of the two flanking arginines in an RRR motif unique to said polypeptide;

b) An α2/δ1 polypeptide comprising an arginine to aliphatic amino acid substitution in at least one of the two flanking arginines in an RRR motif unique to said polypeptide;

c) An α2/δ1 polypeptide comprising an arginine to alanine substitution in at least one of the two flanking arginines in an RRR motif unique to said polypeptide;

d) An α2/δ1 polypeptide comprising a deletion of at least one of the flanking arginines in an RRR motif unique to said polypeptide;

e) An α2/δ1 polypeptide comprising a deletion of up to 9 residues immediately N-terminal to an RRR motif unique to said polypeptide, a deletion of up to 5 residues immediately C-terminal to an RRR motif unique, and a deletion of at least one of the flanking arginines in an RRR motif unique to said polypeptide;

f) An α2/δ1 polypeptide comprising a deletion of up to of up to 9 residues immediately N-terminal to an RRR motif unique to said polypeptide, and a deletion of at least one of the flanking arginines in an RRR motif unique to said polypeptide;

g) An α2/δ1 polypeptide comprising a deletion of up to 5 residues immediately C- terminal to an RRR motif unique, and a deletion of at least one of the flanking arginines in an RRR motif unique to said polypeptide; and

h) An α2/δ1 polypeptide according to a)-g) having at least one conservative amino acid substitution at a position other than a flanking arginines in said RRR motif.

**3**. (Withdrawn) A genetically-modified, non-human mammal, wherein the modification results in a mutated α2/δ1 gene encoding a polypeptide selected from the group consisting of:

a) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has an arginine to non-arginine substitution in at least one of the two flanking arginines in an RRR motif unique to said polypeptide;

b) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has an arginine to aliphatic amino acid substitution in at least one of the two flanking arginines in an RRR motif unique to said polypeptide;

c) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has an arginine to alanine substitution in at least one of the two flanking arginines in an RRR motif unique to said polypeptide;

d) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has a deletion of at least one of the flanking arginines in an RRR motif unique to said polypeptide;

e) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has a deletion of up to 9 residues immediately N-terminal to an RRR motif unique to said polypeptide, a deletion of up to 5 residues immediately C-

terminal to an RRR motif unique, and a deletion of at least one of the flanking arginines in an RRR motif unique to said polypeptide;

f) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has a deletion of up to of up to 9 residues immediately N-terminal to an RRR motif unique to said polypeptide, and a deletion of at least one of the flanking arginines in an RRR motif unique to said polypeptide;

g) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has a deletion of up to 5 residues immediately C-terminal to an RRR motif unique, and a deletion of at least one of the flanking arginines in an RRR motif unique to said polypeptide; and

h) An α2/δ1 polypeptide according to a)-g) having at least one conservative amino acid substitution at a position other than a flanking arginine in said RRR motif; wherein said α2/δ1 polypeptide lacks its leader sequence.

**4**. (Withdrawn) The genetically modified, non-human mammal of claim 3 wherein said wildtype α2/δ1 polypeptide is set forth in SEQ ID NO: 25, 26, 27, 28, 29, 30, or 31.

**5**. (Withdrawn) A genetically-modified, non-human mammal, wherein the modification results in a mutated α2/δ1 gene encoding a polypeptide selected from the group consisting of:

a) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has an amino acid other than arginine at position 215, 217 or both;

b) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has an aliphatic amino acid at position 215, 217 or both;

c) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has an alanine at position 215, 217 or both;

d) An α2/δ1 polypeptide that is identical to a wildtype α2/δ1 polypeptide except that it has a lysine at position 215, 217 or both; and

e) The wildtype mammalian α2/δ1 polypeptide according to A)-d) having at least one conservative amino acid substitution at a position other than residue 215 and 217.

**6**. (Withdrawn) The mammal of claim 2, wherein said mammal exhibits at least one phenotypic characteristic selected from the group consisting of:

a) the phenotypic characteristic of reduced α2/δ1 ligand binding to central nervous system of said mammal;

b) the phenotypic characteristic of reduced gabapentin binding to central nervous system of said mammal;

c) the phenotypic characteristic of reduced analgesic efficacy of an α2/δ1 ligand in said mammal;

d) the phenotypic characteristic of reduced analgesic efficacy of pregabalin in said mammal;

e) the phenotypic characteristic of reduced sedative efficacy of an α2/δ1 ligand in said mammal wherein said mammal is subjected to a sedation test;

f) the phenotypic characteristic of reduced anticonvulsant efficacy of an α2/δ1 ligand in said mammal wherein said mammal is subjected to a sedation test; and

g) the phenotypic characteristic of reduced anxiolytic efficacy of an α2/δ1 ligand in said mammal wherein said mammal is subjected to a sedation test.

**7**. (Withdrawn) The mammal of claim 2, wherein said mammal is a rodent.

**8**. (Withdrawn) The rodent of claim 7, wherein said rodent is a mouse.

**9**. (Withdrawn) The non-human mammal of claim 2, wherein said mammal is homozygous for said modification.

**10**. (Cancelled) An isolated nucleic acid molecule having a sequence encoding a polypeptide comprising the sequence selected from the group consisting of: a) A polypeptide sequence set forth in SEQ ID NO: 17, b) A polypeptide sequence set forth in SEQ ID NO: 18, and c) A polypeptide sequence set forth in SEQ ID NO: 19.

**11**. (Withdrawn) The isolated nucleic acid molecule according to claim 10 a) comprising a nucleotide sequence set forth in SEQ ID NO: 20.

**12**. (Withdrawn) The isolated nucleic acid molecule according to claim 10 b) comprising a nucleotide sequence set forth in SEQ ID NO: 21 or SEQ ID NO: 22.

**13**. (Withdrawn) The isolated nucleic acid molecule according to claim 10 c) comprising a nucleotide sequence set forth in SEQ ID NO: 23 or SEQ ID NO: 24.

**14. (Currently Amended)** A genetically-modified, non-human mammal comprising the nucleic acid **molecule having a** sequence **encoding a polypeptide sequence ~~of claim 10.~~ selected from the group consisting of:**

**a) A polypeptide sequence set forth in SEQ ID NO: 17,**

**b) A polypeptide sequence set forth in SEQ ID NO: 18~~,~~ and;**

**c) A polypeptide sequence set forth in SEQ ID NO: 19.**

**15**. (Withdrawn) A targeting vector for producing a transgenic animal, said vector comprising a nucleic acid having a nucleotide sequence encoding a polypeptide according to claim 2.

**16**. (Withdrawn) A host cell comprising the vector of claim 15.

**17**. (Withdrawn) A genetically-modified animal cell, wherein the modification comprises a mutated gene encoding a polypeptide according to claim 2.

**18**. (Withdrawn) The animal cell of claim 17, wherein said cell is an embryonic stem (ES) cell or an ES-like cell.

**19**. (Withdrawn) The animal cell of claim 17, wherein said cell is isolated from a genetically-modified, non-human mammal containing a modification that results in a mutated gene.

**20**. (Withdrawn) The animal cell of claim 19, wherein said cell is an embryonic fibroblast, stem cell, neuron, skeletal or cardiac muscle cell, myoblast, brown or white adipocyte, hepatocyte, or pancreatic P cell.

**21**. (Withdrawn) The animal cell of claim 17, wherein said cell is murine.

**22**. (Withdrawn) The animal cell of claim 17, wherein said cell is human.

**23**. (Withdrawn) The animal cell of claim 17, wherein said cell is homozygous for said modification.

**24**. (Withdrawn) A method of identifying a gene that demonstrates modified expression as a result of reduced α2/δ1 activity in an animal cell, said method comprising assessing the expression profile of an animal cell containing a genetic modification that disrupts a cα α2/δ1 gene, and comparing said profile to that from a wildtype cell.

**25**. (Withdrawn) The method of claim 24, wherein said cell is homozygous for a genetic modification that disrupts the α2/δ1 gene.

**26**. (Withdrawn) A method of identifying a protein that demonstrates modified expression or post-translational modification as a result of reduced α2/δ1 activity in an animal cell, said method comprising assessing the proteomic profile

of an animal cell containing a genetic modification that disrupts a α2/δ1 gene, and comparing said profile to that from a wildtype cell.

**27**. (Withdrawn) A method of claim 26, wherein said cell is homozygous for a genetic modification that disrupts the α2/δ1 gene.

**28**. (Withdrawn) A method for producing a transgenic animal having a modified response in an α2/δ1 -mediated disorder or activity relative to a wildtype animal, said method comprising: a) transfecting ES cells with a targeting vector for producing a transgenic animal, said vector comprising a nucleic acid having a nucleotide sequence encoding a polypeptide according to claim 2;b) selecting transfected cells undergone homologous recombination; c) implanting said selected transfected cells into blastocysts; d) producing transgenic animals from said blastocysts.

**29**. (Withdrawn) The method of claim 28, wherein said activity or disorder of claim 28 is selected from pain, hyperalgesia, anxiety, sedation, epilepsy, convulsion.

**30**. (Withdrawn) A method for determining whether the physiological effect of a compound on a disorder or activity involves α2/δ1 subunit polypeptide residues that mediate the physiological effect of an α2/δ1 ligand, said method comprising a) providing a first group of mammals according to claim 2 and, a second group of corresponding wildtype mammals, b) treating a first subset of each said group with an α2/δ1 ligand, c) treating a second subset of each said group with a test compound, d) testing each subset for an activity or disorder associated with α2/δ1, and e) comparing the response of each said each said groups and subsets.

**31**. (Withdrawn) The method of claim 30 wherein said activity or disorder of is selected from pain, hyperalgesia, anxiety, sedation, epilepsy, convulsion.

**32**. (Withdrawn) The method of claim 30 wherein said α2/δ1 ligand is gabapentin.

**33**. (Withdrawn) The method of claim 30 wherein said α2/δ1 ligand is pregabalin.

**34**. (Withdrawn) A method for identifying compounds that exert their physiological effect on a disorder or activity through an α2/δ1 subunit polypeptide, said method comprising a) providing a first group of mammals according to claim 2 and a second group of corresponding wildtype mammals, b) treating each said group with a test compound, c) testing each group for an activity or disorder associated with α2/δ1, and d) comparing the response of each said each said groups.

**35**. (Withdrawn) A method for identifying compounds that exert their physiological effect on a disorder or activity through an α2/δ1 subunit polypeptide, said method comprising a) providing a first group of mammals according to claim 2 and a second group of corresponding wildtype mammals, b) treating a first subset of each said group with a ligand that binds an α2/δ1 subunit polypeptide, c) treating a second subset of each said group with a test compound, d) testing each subset for an activity or disorder associated with α2/δ1, and e) comparing the response of each said each said groups and subsets.

**36**. (Withdrawn) The method of claim 35 wherein said ligand is gabapentin.

**37**. (Withdrawn) The method of claim 35 wherein said activity or disorder is selected from pain, hyperalgesia, anxiety, sedation, epilepsy, convulsion.

**38**. (Withdrawn) A method for determining a role of α2/δ1 polypeptide in an activity or disorder, said method comprising a) providing a first group of mammals according to claim 2 and a second group of corresponding wildtype mammals, b) subjecting each said group to a procedure indicative of an activity or disorder, and c) comparing the response of each said group.

**39**. (Withdrawn) The method of claim 38 wherein said activity or disorder of is selected from pain, hyperalgesia, anxiety, sedation, epilepsy, convulsion.

**40**. (Withdrawn) The method of claim 38 wherein said procedure is selected from α2/δ1 ligand binding, gabapentin binding, formalin foot-pad procedure, Tail suspension test, Maximal electro-shock, and Vogel procedure.

**41. (New)** The genetically-modified, non-human mammal of Claim 14 comprising the nucleic acid nucleotide sequence set forth in SEQ ID NO: 20.

**42. (New)** The genetically-modified, non-human mammal of Claim 14 comprising the nucleic acid nucleotide sequence set forth in SEQ ID NO: 21 or SEQ ID NO: 22.

**43. (New)** The genetically-modified, non-human mammal of Claim 14 comprising the nucleic acid nucleotide sequence set forth in SEQ ID NO: 23 or SEQ ID NO: 24.